Published in final edited form as:
Drug Alcohol Depend. 2023 May 01; 246: 109857. doi:10.1016/j.drugalcdep.2023.109857.

Integrating cognitive bias modification for pain and opioid cues into medication for opioid use disorder clinical care: Feasibility, acceptability, and preliminary results

R. Ross MacLean[a,b,*], **Alicia A. Heapy**[a,b], **Andrew J. Waters**[c], **Noah Wolkowicz**[a,b], **Sara K. Szollosy**[a], **Julia Meyerovich**[a,b], **Mehmet Sofuoglu**[a,b]

[a]VA Connecticut Healthcare System, West Haven, CT, USA

[b]Yale University School of Medicine, New Haven, CT, USA

[c]Uniformed Services University of the Health Sciences, Bethesda, MD, USA

Abstract

Background: Despite high co-occurrence, chronic pain is often unaddressed in treatment for opioid use disorder (OUD) and little is known about mechanisms that may underlie associations between pain and opioid use. Using an attentional bias (AB) task with both pain and opioid cues, we evaluated a cognitive bias modification (CBM) task administered during regularly scheduled medications for OUD (mOUD) dosing visits. The current study evaluated the feasibility, acceptability, and preliminary efficacy of the CBM task. Outcomes for AB tasks used traditional mean-based score and trial-level bias scores (TLBS).

Methods: In a double-blind, randomized controlled trial, 28 individuals with OUD and chronic pain engaged in mOUD were randomized to either CBM or an AB control condition and completed up to three tasks per week for four weeks. Standard AB task was completed at baseline and post-treatment. Participants completed feasibility and acceptability measures, and preliminary efficacy (i.e., change in AB) was assessed using ANOVA models.

Results: Participants attended 83.3% of scheduled sessions and generally reported the task was enjoyable, credible, and easy to complete. Preliminary results demonstrated a condition by time interaction highlighting a reduction in AB in the CBM group but not the control group in opioid TLBS variability ($F[1,26]=5.01$, $p = .034$) and pain TLBS towards ($F[1,26]=6.42$, $p = .018$) and pain TLBS variability ($F[1,26]=5.24$, $p = .03$).

*Correspondence to: VA Connecticut Healthcare Center, 950 Campbell Ave 116B, West Haven, CT 06516, USA. ross.maclean@yale.edu (R.R. MacLean).

CRediT authorship contribution statement

RRM, MS, AAH, and AJW designed the study. RRM implemented the study procedures. NRW and RRM conducted statistical analysis. SKS and JM assisted with drafting the manuscript. All authors contributed and have approved the final manuscript.

Declaration of Competing Interest

The authors have no conflicts of interest to report.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.drugalcdep.2023.109857.

Conclusions: The current study supports integrating brief, computer-based tasks designed to reduce AB into mOUD clinical care. The preliminary results suggest that TLBS outcomes may be more sensitive to capture changes in AB; however, larger studies are required.

Keywords

Opioid use disorder; Chronic pain; Attendonal bias; Cognitive bias modification; Methadone; Buprenorphine

1. Introduction

From May 2020 to April 2021, the 12-month incidence of drug overdose deaths surpassed 100,000 for the first time, with nearly two-thirds of deaths involving synthetic opioids other than methadone (O'Donnell et al., 2021). Medications for opioid use disorder (mOUD), including methadone and buprenorphine, are the clear first line treatment option and have been shown to reduce mortality and improve psychosocial outcomes (National Academies of Sciences, 2019). In an effort to improve engagement in mOUD, there has been a call to treat co-occurring conditions that may interfere with treatment goals (Novak et al., 2019). Chronic pain is one such condition that may be particularly important to address in mOUD treatment. Even with engagement in mOUD, rates of chronic pain remain high among individuals with OUD (Dunn et al., 2015; Hser et al., 2017). Recent research suggests that chronic pain is rarely managed through mOUD care, but is a driving factor in return to opioid use (Ellis et al., 2021). Taken together, it is important to develop brief, complementary treatments that can be integrated into existing mOUD care.

Automatic cognitive processes are believed to play an important role both in substance use disorders and chronic pain (Wiers and Stacy, 2006). One such process, attentional bias (AB), occurs when a particular cue type (e.g., opioid or pain-related cues) becomes flagged as "salient" and grabs and holds the attention in preference to other cues in the environment (Robinson and Berridge, 1993). The automatic capture of drug-related cues can increase craving which, in turn, increases the salience of drug-cues in the environment and initiates drug-seeking behavior (Franken, 2003). Although there are mixed results for AB in individuals who use alcohol and tobacco, a meta-analysis revealed a robust AB to opioid cues in individuals who use opioids, even among those engaged in mOUD (MacLean et al., 2018). Likewise, in studies of chronic pain patients, AB toward pain cues is present early in the attentional process (i.e., ≤500 ms) (Todd et al., 2015). Chronic pain patients with a greater AB for pain cues also report greater acute intensity and interference of pain (Van Ryckeghem et al., 2013). The relationship between AB for pain cues and opioid urges has not been examined in OUD patients receiving mOUD. Similar to opioid cues, hypervigilance for pain-related stimuli in individuals with OUD may contribute to opioid craving and drug-seeking behaviors. As such, interventions that target attention to both opioid and pain cues could improve mOUD treatment outcomes.

Cognitive bias modification (CBM) refers to the use of tasks intended to change AB, and by extension, behaviors associated with increased AB. These tasks were initially developed as a cognitive intervention to reduce vigilance to threatening stimuli in anxiety disorders

(MacLeod and Clarke, 2015). A recent Delphi consensus study highlighted the high clinical potential of CBM for substance use disorders, especially when administered multiple times per week as an adjunct to ongoing treatment (Verdejo-Garcia et al., 2022). A study in individuals who use opioid engaged in mOUD reported that, compared to a control task, completing three sessions of CBM training for opioid cues reduced AB and was associated with fewer lapses within 2 months post-treatment (Ziaee et al., 2016). To date, CBM for pain cues has only been evaluated in chronic pain patients and results suggest that CBM is associated with improvements in pain severity, interference, and anxiety about pain (Carleton et al., 2011; Schoth et al., 2013; Sharpe et al., 2012). Despite growing interest in CBM for both drug (Field et al., 2014) and pain (Cox et al., 2014; Todd et al., 2016) stimuli, some researchers have suggested that inconsistent findings in the effectiveness of CBM dampens enthusiasm (Christiansen et al., 2015; Field et al., 2014; Mogoase et al., 2014). Of note, these researchers advocate for more rigorous clinical trials that include randomization and adequate controls (Christiansen et al., 2015; Field et al., 2014). Use of CBM is not intended to replace mOUD or other evidence-based OUD treatments; rather, CBM could offer a brief, low-burden intervention that can be administered over a number of sessions to potentially increase the efficacy or engagement in established interventions.

The present study is a pilot randomized controlled trial in which Veterans with OUD engaged in mOUD were randomized to receive up to 12 sessions of CBM or a standard AB task (control). To our knowledge, this is the first study to evaluate contemporaneous AB to opioid and pain cues and evaluate CBM for both cue types in individuals with OUD engaged in mOUD. The primary aim of the study was to evaluate the feasibility and acceptability of administering a brief CBM task at mOUD dosing visits. We also sought to evaluate the preliminary efficacy of CBM to reduce AB for pain and opioid cues. We hypothesized that participants would complete at least 50% of scheduled treatment visits and would report the task was easy to complete and satisfying. We also hypothesized that AB to both opioid and pain cues would be reduced at post-treatment in the CBM, but not the AB control, group and participants would rate the cues in the AB tasks as salient.

2. Materials and methods

2.1. Participants

Participants were 28 adults receiving mOUD in the Opioid Treatment Program at VA Connecticut Healthcare System. Eligibility criteria included: at least three scheduled appointments for mOUD dosing per week and reporting at least moderate pain for the past 3 months. The requirement for scheduled dosing was intended to evaluate CBM as an add-on to an existing clinical encounter. Exclusion criteria included: characteristics that would impair ability to read pain/opioid cues in the AB task (i.e., uncorrected defective vision or an inability to read, write, or speak English) and/or increased probability of inpatient treatment (i.e., untreated major psychiatric disorder or substance use disorder that requires inpatient detoxification). Participants were recruited from February 2019 to June 2021. This trial was registered on ClinicalTrials.gov (NCT04132609). Due to COVID restrictions research was paused from March 2020 to October 2020. Participants were recruited from flyers posted in the clinic and opt-in letters sent to every Veteran with ≥3 scheduled dosing visits per week.

2.2. Procedures

2.2.1. Baseline and randomization—During the baseline visit, participants were consented and then completed the baseline AB task (see 2.2.3.1. below) and were randomly assigned via urn randomization to either CBM or AB control. Randomization sequence was generated using a Microsoft Access program and was stratified by self-reported sex (i.e., male or female) and mOUD type (i.e., buprenorphine or methadone). Research staff and participants were blind to the study condition. Study staff not involved in data collection coded conditions as "A" and "B". Participants were told that one condition was intended to reduce attention to opioid and pain cues, but were not informed of any differences between the AB tasks. See the CONSORT diagram in Supplemental Materials, S.1.

2.2.2. Interventions—After the baseline visit, participants were scheduled to meet with a researcher to complete interventions during regularly scheduled dosing visits at least 3 times per week for 4 weeks (up to 12 administrations). Participants would present the clinic, receive mOUD dose, then complete the intervention task.

2.2.2.1. Attentional bias task (Control).: Attentional bias task was administered using a dot-probe task in E-Prime (Pittsburgh, PA) based on a modified version from the Attentional Bias Measurement ToolBox (Abend et al., 2014). A set of 40 pairs of pain and neutral words and 40 pairs of opioid and neutral words were presented twice each (160 trials total). Location of the probe and words (i.e., top and bottom) were counterbalanced within each administration, and selection of trial type (pain/neutral or opioid/neutral) was random throughout the task. At the start of each trial, a fixation cross was presented for 500 ms, followed by the presentation of a pain-neutral or opioid-neutral word pair for 500 ms. A "p" or a "q" replaced either the salient (i.e., pain/opioid) or neutral word. Using the keyboard, participants were asked to respond as fast as possible when a "p" or "q" replaced the word. A 500 ms inter-trial interval occurred after each participant's response. Opioid (e.g., needle, high), and pain sensory (e.g., throbbing, burning) and affective (e.g., tiring, unbearable) words were taken from prior research demonstrating AB in OUD (Marissen et al., 2006; Ziaee et al., 2016) and chronic pain patients (Carleton et al., 2011; Todd et al., 2016), respectively. Word pairs were matched for length and frequency of use in the English language (See Supplemental Materials, S.2).

2.2.2.2. Cognitive bias modification.: The CBM task was identical to the AB control except that the probe always replaced the neutral cue on both pain/neutral and opioid/neutral trials.

2.2.3. Post-treatment—During week 5, participants completed measures assessing treatment credibility and satisfaction, and the AB task. As a validity check, participants were asked if they knew what condition they were assigned, and were asked open-ended questions regarding the opioid and pain words used in the AB task. Participants were asked to reflect on the task they completed during the study and respond to the following questions: 1) "What are your thoughts about the words related to pain?"; 2) "What are your thoughts about the words related to opioids?".

2.3. Primary outcomes

Satisfaction was assessed by inquiring whether “The task was enjoyable” and ease of use was evaluated with two items: 1) “The task was easy to learn how to use” and 2) “The task was difficult.” Responses to these items used a 5-point Likert scale anchored by “Strongly Disagree” and “Strongly Agree.” Treatment credibility was evaluated using a modified version of the Treatment Credibility Scale (Borkovec and Nau, 1972) containing 7 items assessed on a 10-point scale and evaluated at post-treatment. The seven items dealt with: 1) How logical the treatment seemed, 2) confidence it would help with pain and 3) craving, 4) if they would recommend treatment to a friend with a pain or 5) opioid problem, and 6) how successful the treatment was in helping with pain and 7) opioid craving. Credibility ratings for each question were summed to create a total score.

2.4. Preliminary efficacy

After data cleaning (see Supplemental Materials, S.3.), a mean bias score was calculated by subtracting the overall mean reaction time from congruent pain and opioid trials (i.e., probe located behind the pain or opioid word) from the mean reaction time across incongruent trials (i.e., probe behind the neutral word). A greater mean bias score is indicative of a greater AB towards opioid and pain cues. Despite being the standard method of scoring AB tasks, recent research has highlighted poor psychometric properties of the mean bias score (Emery and Simons, 2015; Jones et al., 2018; Rodebaugh et al., 2016). The trial-level bias score (TLBS) offers an alternative to the mean bias score that considers potential temporal fluctuations in AB by subtracting temporally adjacent pairs of incongruent and congruent trials (Zvielli et al., 2015). Prior research has demonstrated that, compared to the mean bias score, the TLBS has superior reliability in substance use populations (Jones et al., 2018; Yang et al., 2022). There are five TLBS indices separated into 3 indices (i.e., toward, away, and variability). A greater TLBS toward indicates a greater AB toward opioid and pain cues (i.e., TLBS > 0 ms), while a greater TLBS away represents a greater tendency to divert attention from opioid and pain cues (i.e., TLBS < 0 ms). The third index, variability, characterizes the stability of AB and is calculated by the average of the absolute values of sequential differences in TLBSs. In general, greater TLBS variability is indicative of less stability of TLBS toward or away over time.

2.5. Analytic plan

We first evaluated any demographic differences between treatment groups using standard t-tests (continuous variables) and chi-squared tests (categorical variables). Then we tabulated attendance to task administration appointments and calculated the average administration time for the baseline and post-treatment AB tasks. Summary descriptives were calculated for satisfaction and credibility measures.

Mean bias, mean TLBS toward, mean TLBS away, and TLBS variability were used as AB outcome variables. Distribution of raw data from all AB outcomes met general assumptions of normality (Hair et al., 2010; see Supplemental Materials S.4.). We conducted separate mixed design ANOVAs for each cue-type (pain or opioid) with one between-person factor (group; CBM and control) and one within-person factor (time; pre- and post-treatment) for each AB outcome. Consistent with our hypotheses, our analysis was focused on the

group-by-time interaction to evaluate for preliminary efficacy of CBM to reduce AB to salient cues. AB outcome data and analysis code are available at (https://osf.io/b9q3c/). Data were analyzed using R 4.2.2, and the packages Tidyverse 1.3.2 (Wickham et al., 2019), *itrak* 0.0.0.9999 with the nearest options (Beevers et al., 2019), and afex 1.1–1. Type I error rate was set at alpha = .05.

3. Results

3.1. Descriptive statistics

The 28 participants primarily identified as male (90%) with a mean age of 50.3 (SD = 12.2) and the majority identifying as White (n = 22) followed by Mixed/other (n = 4), and Asian (n = 2). Most (n = 26) participants were receiving methadone and only 2 were receiving buprenorphine. There were no significant differences between treatment groups with respect to demographic variables (*ps* >.22; Supplemental Materials, S.5.). At baseline and post-treatment, participants took an average of 4:37 (*SD* = 0:37) and 4:30 (*SD* = 0:44) minutes, respectively, to complete the AB task.

3.2. Primary outcome

A total of 15 participants were randomized to CBM and 13 were randomized to AB control. Participants attended an average of 10 out of 12 possible treatment sessions (83.3%) with no differences by group assignment [$t(26) = 0.36$, $p = .72$]. Most perceived the task as neutral (n = 13); however, more participants agreed the task was enjoyable (n = 11) versus those that disagreed (n = 4) (Fig 1a). The majority of participants agreed (n = 12) or strongly agreed (n = 14) the task was easy to complete with only 2 participants disagreeing (Fig. 1b). Most participants also strongly disagreed (n = 11) or disagreed (n = 11) the task was difficult, 4 rated the task as neutral, and 2 strongly agreed the task was difficult (Fig. 1c). Overall treatment credibility was in the moderate range (M = 35.2, *SD* = 16.7) with excellent reliability (Cronbach's Alpha=.92).

3.3. Preliminary efficacy

Summary statistics for all AB outcomes can be found in Supplemental Materials, S.4. Results for preliminary efficacy models can be found in Table 1. Our interpretation is focused on models with a significant time by group interaction as preliminary efficacy for CBM to reduce AB to pain and opioid cues. For opioid cue trials, only TLBS variability exhibited a significant time-by-group interaction with significantly less stability (i.e., greater AB) pre-post cue presentation in the control condition compared to the CBM condition (Fig. 2a). For pain cues, mean TLBS toward and TLBS variability for pain cues exhibited a significant time-by-group interaction. For pain TLBS toward, there was a significant reduction in AB toward pain cues pre-post cue presentation in the CBM condition compared to the control condition (Fig. 2b). For pain TLBS variability, there appeared significantly less stability (i.e., greater AB) pre-post cue presentation in the control condition compared to the CBM condition (Fig. 2c). For all of these outcomes, a significant Levene's test indicated unequal variances between treatment groups. Therefore, we ran post-hoc Welch's t-tests as robust comparisons of pre and post outcomes in each group. For opioid TLBS variability, results were not significant comparing pre-CBM and pre-control assessments ($t(25.8) =$

1.21, $p = .24$), but were significant when comparing post measures ($t(16.4) = 2.96$, $p = .009$). For pain TLBS toward, results were not significant comparing pre-CBM and pre-control assessments ($t(25.2) = .02$, $p = .84$), but were significant when comparing post measures ($t(13.8) = 2.87$, $p = .013$). For pain cues, results were not significant comparing pre-CBM and pre-control assessments ($t(24.4) = 0.95$, $p = .35$), but were significant when comparing post measures ($t(13.8) = 2.63$, $p = .020$). In all of the above outcomes, the direction of the effects are consistent with a post-treatment decrease in AB in the CBM but not in the control group.

3.4. Validity check

Overall, 82% (n = 23) reported they were “unsure” what condition they were in, 2 participants correctly guessed they were in active treatment, 2 correctly guessed they were in control, and 1 participant randomized to control guessed they were in active. Interestingly, when asked for their thoughts on words used as cues during AB tasks, very few participants could recall any pain words. In contrast, the words associated with opioid use were often perceived as extremely salient (see Table 2 for exemplar qualitative statements). Verbatim responses to validity queries for each participant can be found in Supplemental Materials, S.6.

4. Discussion

The results of this study suggest that adding a brief AB task to a mOUD visit was acceptable and feasible. Average completion of task visits was high (i.e., 83.3%) and participants generally rated the task as enjoyable and easy to complete. Preliminary results suggest that the CBM group (versus AB control) demonstrated a reduction in AB for pain cues and opioid cues over the course of 4 weeks. These differences were apparent using the TLBS toward and variability AB outcomes, but not with the more traditional mean bias score. Recent research exploring AB for smoking cues in individuals who use tobacco reported that split-half and test-retest reliability for mean bias score was non-significant across three repeated administrations, but was high (i.e.,.79 to.95) for all TLBS indices (Yang et al., 2022). A meta-analysis of AB variability revealed that, compared to controls, (sub)clinical samples demonstrated increased variability ($g = 0.462$) in disorder specific AB tasks (Todd et al., 2022). Little is known about the how individuals with OUD may differentially perceive specific cues related to opioids or pain. Prior research generally supports that pain cues are perceived as threatening or aversive in individuals with chronic pain (Todd et al., 2015). Drug cues, however, could be both appetitive and/or aversive in individuals with OUD (Franken et al., 2003). Reactivity to these cues may be mediated by different brain regions, as demonstrated in human fMRI studies (Stewart et al., 2019). Furthermore, all of the study participants were actively involved in mOUD treatment for different lengths of time and with varying doses of methadone/buprenorphine. Prior studies have shown that individuals engaged in treatment may have lower responses to drug cues compared to those who are not in treatment (Wilson et al., 2004); which may explain an effect of CBM on only one opioid AB outcome. All of the participants were experiencing at least moderate chronic pain despite difference in mOUD treatment characteristics.

Prior CBM research has used the mean bias score with multiple task administrations. For example, up to eight sessions of CBM for pain cues in individuals with chronic pain was associated with a significant reduction in pain intensity, anxiety, depression, and pain interference (Schoth et al., 2013). Using a median bias score (similar to mean bias score), a large study of 1405 individuals with alcohol use disorder that completed up to 6 sessions of CBM tasks for alcohol cues found a slight reduction in relapse rates at 1 year compared to control tasks; however, the change in median bias score was not related to clinical findings (Rinck et al., 2018). Indeed, tasks designed to modify AB to drug cues have shown inconsistent effects on change in AB for drug-related cues from baseline (Heitmann et al., 2018). Despite one study demonstrating success with CBM as an adjunctive treatment to mOUD (Ziaee et al., 2016), another study in individuals with OUD receiving mOUD evaluated a one-time administration of a CBM task and found no immediate differences in AB (Charles et al., 2015). To date, no studies have evaluated CBM for drug or pain cues using the TLBS outcomes. The current results suggest that certain TLBS outcomes may be sensitive to detect changes in AB after repeatedly completing tasks designed to modify AB.

To the authors' knowledge, this is the first study to contemporaneously evaluate AB to pain and opioid cues in the context of mOUD treatment. There is ample empirical evidence for the presence of severe pain in individuals with OUD (Ellis et al., 2021), and the presence of both OUD and chronic pain is associated with increased clinical complexity (MacLean et al., 2021a); but very little is known about implicit attentional resources associated with pain in individuals with OUD. In chronic pain samples, pain is associated with subsequent opioid use, and those at high risk for misuse tend to take larger doses of opioids, but experience smaller subsequent decreases in pain (Carpenter et al., 2019). Among individuals with OUD engaged in mOUD, the relationship between chronic pain and opioid use is less clear (MacLean et al., 2021b). Recent research using mobile surveys has suggested that reports of daily pain are high in individuals with OUD (i.e., 70%) and the relationship between momentary pain and subsequent opioid use is mediated by momentary craving (Mun et al., 2021). Given the hypothesized role of AB as a precursor to craving, it may be that increased attention to pain and/or opioid cues could increase craving and subsequent use. For example, using a mobile version of the drug-Stroop task with cocaine and heroin cues found that individuals with OUD demonstrated increased AB for both drug cues and drug-cue AB was elevated one hour prior to conscious report of craving in daily life (Waters et al., 2012). Prior research has demonstrated success assessing AB for two cue types using a mobile device in a population with alcohol and tobacco use (MacLean et al., 2020). Studies evaluating naturalistic AB to pain and opioid cues may help clarify the possible role of AB to pain cues and opioid craving and use during daily life.

Given the preliminary findings of a reduction in AB for pain cues, it is interesting that very few participants could recall pain cues in the post-treatment validity check. The proposed Threat Interpretation Model states that the attentional resources captured by cues may depend on the level of threat in individuals with chronic pain (Todd et al., 2015). Specifically, the initial orientation (200–500 ms) is increased as the level of threat increases (e.g., higher AB); however, sustained attention (>1000 ms) results in difficulty disengaging with moderate threat (e.g., higher AB) but avoidance under conditions of low or high threat (e.g., lower AB) (Todd et al., 2015). In the current study, it is possible that recall

for sensory and affective pain cues may be overshadowed by the attentional salience of opioid cues in the same task. Prior research has suggested that individuals with chronic pain receiving opioids exhibit an AB for pain cues presented for 2000 ms, but not 200 ms (Garland and Howard, 2013). This potentially highlights an inability for individuals with chronic pain to disengage with threatening painful stimuli presented for longer intervals. Given reports of elevated fear of pain-related withdrawal in individuals with OUD receiving mOUD (Bentzley et al., 2015; Winstock et al., 2011), the initial attention (e.g., 500 ms) may be especially salient and possibly modifiable to improve pain outcomes.

The current study has several notable limitations. First, the primary focus of the study was to determine whether administering a cognitive training task as an adjunctive treatment was feasible and acceptable. The influence of receiving mOUD immediately prior to completing AB tasks is not known. It is possible that AB to opioid or pain cues would be different if measured hours after mOUD administration or outside of a clinical environment. Despite pre-processing efforts to eliminate outlier responses, there was still significant variability in AB outcomes between groups. Robust t-tests generally support model results, but preliminary efficacy findings will need to be replicated in a larger clinical sample. Analysis of two cue types during AB is conceptually novel, but has not been widely studied using traditional mean bias score or TLBS outcomes. More research is needed to evaluate possible differences in single versus dual cue AB paradigms. The effect sizes in the current study are relatively small and administering AB tasks more frequently, using a blocked design by cue type, or explicitly targeting individuals with high baseline AB for opioid and/or pain cues may strengthen the effect of CBM. Finally, use of the TLBS has been shown to have superior reliability compared to mean bias score in populations with a substance use disorder (Yang et al., 2022); however, this does not ensure that the TLBS outcomes have adequate external validity. Additional studies are necessary to establish construct validity for TLBS outcomes in individuals with OUD receiving mOUD.

The current study supports integrating brief, computer-based tasks designed to reduce AB into regular clinical care. The preliminary efficacy results are promising, and suggest the use of TLBS outcomes may be more sensitive to capture changes in AB. Future research should explore external validity of AB for opioid and pain cues as well as whether change in AB is associated with commensurate changes in related clinical phenomena. New methods of evaluating AB that include assessment using mobile devices could increase utility and clinical relevance of tasks designed to modify AB (Cox et al., 2014) and dual cue AB has been effectively evaluated in addiction samples using a mobile devices. The current results underscore the possibility of modifying attentional resources that could impact the experience or expression of opioid and/or pain-related phenomena.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Role of funding source

Support for Dr. MacLean was provided by a VA VISN1 Career Development Award and a VA Clinical Science Research and Development Career Development Award (1IK2CX002286). The New England Mental Illness

Research, Education, and Clinical Center (MIRECC) and VA Connecticut Healthcare System helped support the project. The content is solely the responsibility of the authors and does not necessarily represent the official views of the Department of Veterans Affairs.

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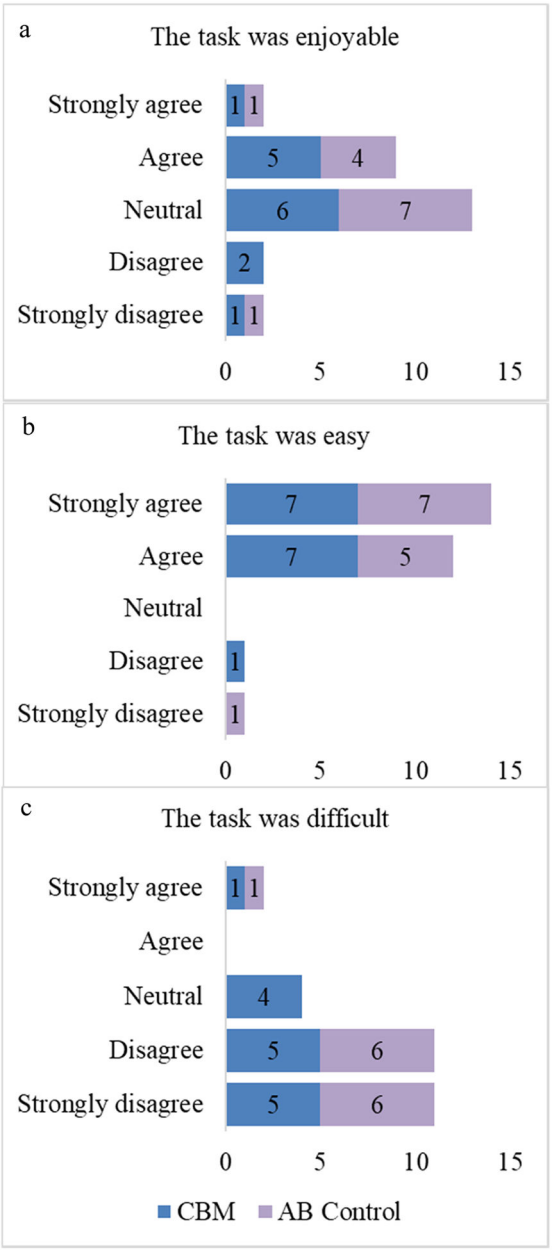

Fig. 1.

Post-treatment satisfaction and ease of use for CBM and AB control groups. *Note:* CBM = Cognitive bias modification; AB = Attentional bias.

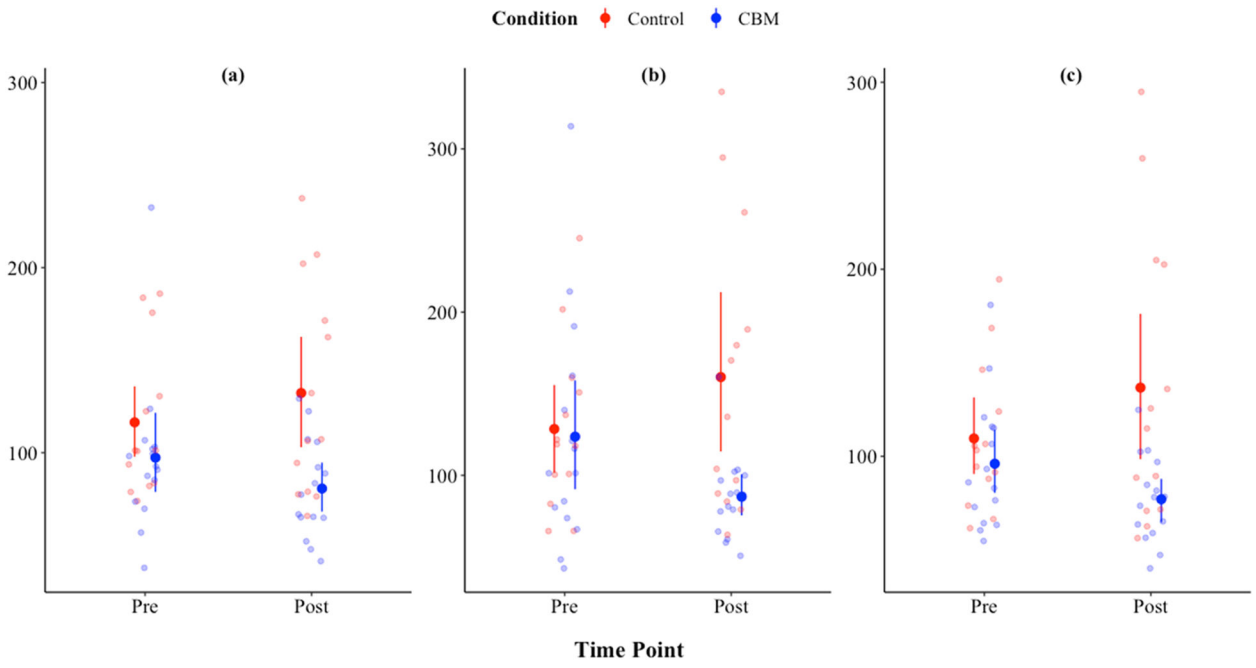

Fig. 2.

Trial level bias score significant condition by time interactions. *Note*: Significant interactions for (a) opioid trial-level bias variability, (b) pain trial-level bias towards, and (c) pain trial-level variability. Bars represent 95% bootstrapped confidence intervals. Large dots represent group means; small dots represent individual data points. CBM = “Cognitive Bias Modification”.

Table 1

ANOVA mixed model statistics by attentional bias cue type.

	Opioid Cues			**Pain Cues**		
Mean Bias	**F (1,26)**	**p-value**	η^2_G	**F (1,26)**	**p-value**	η^2_G
Condition	3.39	.077	.048	0.08	.786	.001
Time-Point	3.01	.095	.066	1.54	.226	.029
Condition*Time-Point	0.55	.466	.013	0.94	.342	.018
Mean TLBS Toward	**F (1,26)**	**p-value**	η^2_G	**F (1,26)**	**p-value**	η^2_G
Condition	**6.94**	**.014**	**.153**	4.21	.050	.147
Time-Point	0.03	.859	<.001	0.03	.865	.006
Condition*Time-Point	2.29	.142	.028	**5.45**	**.028**	**.052**
Mean TLBS Away	**F (1,26)**	**p-value**	η^2_G	**F (1,26)**	**p-value**	η^2_G
Condition	**4.63**	**.041**	**.119**	**4.32**	**.048**	**.107**
Time-Point	2.17	.153	.020	0.50	.486	.005
Condition*Time-Point	0.89	.354	.008	2.59	.120	.027
TLBS Variability	**F (1,26)**	**p-value**	η^2_G	**F (1,26)**	**p-value**	η^2_G
Condition	**5.90**	**.022**	**.154**	**5.58**	**.026**	**.136**
Time-Point	0.00	.955	<.001	0.19	.666	.002
Condition*Time-Point	**5.01**	**.034**	**.037**	**6.12**	**.020**	**.059**

Note: "Mean Bias" refers to the traditional approach to examining attentional bias by averaging across all reaction times. TLBS = Trial Level Bias Score. Bolded numbers indicate significant effects at $p < .05$. η^2_G = generalized eta-squared.

Table 2

Qualitative responses to open-ended validity questions.

	Opioid Cues	Pain Cues
CBM	"Yeah I found myself sometimes, just like if an opioid word came up that I would be focused on that word and then come back to looking for the p or q, so it's almost like my brain deviated from the ultimate goal of finding the p or q and got trapped in the opioid word." (101) "It was just kind of just grab my attention like the word 'bundle' or 'heroin' or whatever it was just the words related to opiates stand out to me … they just grabbed my attention more" (116) "They really just popped out to me" (117) "It was attracting the cravings I didn't like them" (124) "I didn't really notice whether it was a p or a q or anything what word was associated with it, I didn't really see the words; fentanyl, opiates heroin, there was a bunch of them in there." (130)	"I wasn't paying attention for the pain words which I should've been now that you mention it you know but I just noticed the dope words popped up more often than the pain words." (113) "Those words I didn't even give it a thought, no meaning whatsoever" (118) "No, I notice more of the words related to like heroin usage" (125) "I don't remember words related to pain I mostly remember the drug words" (127) "They had no effect on me" (131)
AB	"As soon as they came up, I noticed you know heroin boom just slapped me in the face" (100) "They stuck out more, I paid more attention to them, I didn't really tend to notice the rest of the words until it was words about drugs" (115) "Yeah, I'd give it like a little giggle or something because I haven't seen that word in a long time you know smack overdose, I definitely saw those words. As far as the pain words for some reason they didn't focus on my brain." (132) "It brought up a lot of old memories. And basically helped remind me of how far I've come when it comes to recovery." (108)	"I mostly noticed the drug words … To be honest. I didn't even focus on the pain words that's interesting" (100) "You know I didn't notice them as much as I noticed the drug related words" (102) "I'm surprised because I can't remember any of the words that relate to the pain. That's really odd because I've got a really good memory, which it's really blowing me away." (126) "They didn't affect me. … Not too many, the drug part I recognize all those words the ones related to pain I didn't really even see any I don't think" (132)
Control	"No, I thought it was funny. That's what I was saying, when I was reading the words I was seeing, you know, "dope" and various words that would be related to drug use and it made me chuckle" (111)	"There was a lot of them in there, it kind of made me want to use honestly because I had seen the words a lot, you know what I mean." (128)

Note: Participants were queried during post-treatment session and asked the following questions: 1) "What are your thoughts about the words related to pain?"; 2) "What are your thoughts about the words related to opioids?" Number in parentheses indicates the participant ID. Full list of participant responses can be found in Supplementary Materials, S.6.